

04-05-06

ILM
PATENT
674543-2001.5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Walker et al.
Serial No. : 10/081,787
Filed : February 22, 2002
For : REGULATION OF INTRACELLULAR
GLUCOCORTICOID CONCENTRATION
Examiner : Shobha Kantamneni
Group Art Unit : 1617



745 Fifth Avenue, New York, NY 10151

EXPRESS MAIL

Mailing Label Number: EV 746685164 US

Date of Deposit: April 4, 2006

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" Service under 37 CFR 1.10 on the date indicated above and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Charles Jackson
(Typed or printed name of person mailing paper or fee)

Charles Jackson
(Signature of person mailing paper or fee)

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The Examiner's attention is respectfully directed to the following documents set forth in the accompanying form PTO-1449, which is provided in duplicate. A copy of the cited documents is enclosed. Applicants request that the Examiner consider and make of record the documents cited herein and that the Examiner return an initialed copy of the Form PTO-1449 to the Applicant's attorneys.

This Information Disclosure Statement is not a representation that the documents cited herein is considered most pertinent, or that a search has been undertaken or that the cited documents are indeed prior art. The Examiner is invited to undertake an independent search.

04/06/2006 WASFAW1 00000062 10081787

01 FC:1806

180.00 OP

1

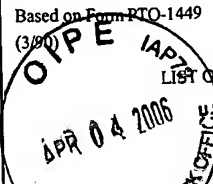
00354508

As this Information Disclosure Statement is being submitted after receipt of a non-final Office Action, a check in the amount \$180.00 is enclosed in payment of the fee for consideration and entry of this document as set forth in 37 C.F.R. 1.17(p).

As these documents present no new issues to patentability, it is respectfully requested that the Examiner considers and make of record the documents cited herewith and that a copy of Form PTO-1449 be initialed by the Examiner and returned to the undersigned.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: Thomas J. Kowalski by Angela M. Collison
Thomas J. Kowalski
Reg. No. 32,147
Angela M. Collison
Reg. No. 51,107
(212) 588-0800.

Based on Form PTO-1449 (3/99) 	ATTY. DOCKET NO. 674543-2001.5	SERIAL NO. 10/080,787
	APPLICANT Brian Robert Walker	
	FILING DATE February 22, 2002	GROUP 1617

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AA	5,128,150	7/7/1992	Edward Shanbrom			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
AB	97/07789	03/06/1997	WIPO				

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

AC	ACTH; Adrenocortical Steroids: Inhibitors Of Biosynthesis, Chapter 63, p. 1463-1473
AD	International Classification Of Diseases - 10 (1992); pgs. 332-337
AE	Endocrinology and Metabolism, Part Thirteen, Chapter 335, p. 1960-1965
AF	Anil K. Agarwal, et al., Cloning And Expression Of Rat cDNA Encoding Corticosteroid 11 β -Dehydrogenase, Journal of Biological Chemistry (1989), Vol. 364, No. 32, p. 18939-18943
AG	Olusola A. Ajilore, et al., In Vivo Characterization Of 11 β -Hydroxysteroid Dehydrogenase In Rat Hippocampus Using Glucocorticoid Neuroendangerment As an Endpoint, Neuroendocrinology (1999): 69, p. 138-144
AH	Robert C. Andrews, et al., Effects Of the 11 β -Hydroxysteroid Dehydrogenase Inhibitor Carbenoxolone On Insulin Sensitivity In Men With Type 2 Diabetes, Journal of Clinical Endocrinology & Metabolism (2003): 88, (1), p. 285-291
AI	J.A. Attea, et al., Early Morning Hyperglycaemia "Dawn Phenomenon" In Non-Insulin Dependent Diabetes Mellitus (NIDDM): Effects Of Cortisol Suppression By Metyrapone, Diabetes Research (1990): 14, p. 181-185
AJ	C.G. Beardwell, et al., Prolonged Remission In Florid Cushing's Syndrome Following Metyrapone Treatment, Clinical Endocrinology (1981): 14, p. 485-492
AK	Andrew S. Brem, et al., Bidirectional Activity Of 11 β -Hydroxysteroid Dehydrogenase In Vascular Smooth Muscle Cells, Steroids (1995): 60, p. 406-410
AL	C. Calle, et al., Decreased Insulin Binding And Antilipolytic Response In Adipocytes From Patients With Cushing's Syndrome, Bioscience Reports (1987) Vol. 7, No. 9, p. 713-718
AM	C. Calle, et al., Binding And Antilipolytic Action Of Insulin In Isolated Adipocytes From Cortisol-Treated Rats, Revista Espanola De Fisiologia (1988) Vol. 44, No. 3, p. 309-314
AN	S. Diederich, et al., In The Search For Specific Inhibitors Of Human 11 β -Hydroxysteroid-Dehydrogenases (11 β -HSDs): Chenodeoxycholic Acid Selectively Inhibits 11 β -HSD-I, European Journal Of Endocrinology (2000) Vol. 142, p. 200-207
AO	J. Donckier, et al., Successful control Of Cushing's disease In the Elderly With Long Term Metyrapone, Postgraduate Medical Journal (1986) Vol. 62, p. 727-730
AP	D. Englehardt, et al., Therapy Of Cushing's Syndrome With Steroid Biosynthesis Inhibitors, J. Steroid Biochem. Molec. Biol. (1994) Vol. 49, No. 4-6, p. 261-267
AQ	J. Fain, et al., Effects Of Glucocorticoids On Metabolism Of Adipose Tissue In Vitro, The Journal Of Biological Chemistry (1963) Vol. 238, No. 1, p. 54-58
AR	Pietro Gareri, et al., Antiabsence Effects Of Carbenoxolone In Two Generic Animal Models Of Absence Epilepsy (WAG/Rij rats and <i>lh/lh</i> mice), Neuropharmacology (2005) Vol. 49, p. 551-563
AS	A. Golay, et al., Evolution From Obesity To Diabetes, Diabete & Metabolisme (Paris) (1994): 20, p. 3-14
AT	J.A. Gomez-Capilla, et al., Effect Of Insulin And Carbenoxolone On Adrenaline Stimulated Lipolysis In Human Lipoma, Horm. Metab. Res. (1990): 22, p. 551-552
AU	J.A. Gomez-Capilla, et al., Effect Of Carbenoxolone On Glucose Metabolism In Rat Adipose Tissue (1988) Vol. 37, No. 7, p. 1299-1301
AV	Elise P. Gomez-Sanchez, et al., Central Hypertensinogenic Effects Of Glycyrrhizic Acid And Carbenoxolone, Am. J. Physiol (1992): 263, (Endocrinol. Metab. 26) p. E1125-E1130
AW	Paul Grinberg, et al., Effect Of Metyrapone On Insulin, Cortisol, And Glucose Tolerance Test Responses In Diabetes, New York State Journal Of Medicine (1970) p. 2341-2343
AX	Muhammad M. Hammami, et al., Regulation Of 11 β -Hydroxysteroid Dehydrogenase Activity In Human Skin Fibroblasts: Enzymatic Modulation Of Glucocorticoid Action, Journal of Clinical Endocrinology and Metabolism (1991) Vol. 73, No. 2, p. 326-334

EXAMINER

DATE CONSIDERED

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Based on Form PTO-1449 (3/90) LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)	ATTY. DOCKET NO. 674543-2001.5	SERIAL NO. 10/080,787
	APPLICANT Brian Robert Walker	
	FILING DATE February 22, 2002	GROUP 1617

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

	AY	H. Hauner, et al., Glucocorticoids And Insulin Promote The Differentiation Of Human Adipocyte Precursor Cells Into Fat Cells, Journal of Clinical Endocrinology and Metabolism (1987), Vol. 64, No. 4, p. 832-835
	AZ	A. Holmang, et al., The Effects Of Cortisol On Insulin Sensitivity In Muscle, Acta, Physiol Scand (1992): 144, p. 425-431
	BA	B. Jeanrenaud, et al., Studies On Rat Adipose Tissue In Vitro, Journal of Biological Chemistry (1960) Vol. 235, No. 8, p. 2217-2223
	BB	W. J. Jeffcoate, et al., Metirapone In Long-Term Management Of Cushing's Disease, British Medical Journal (1977): 2, p. 215-217
	BC	P. H. Jellinck, et al., Differential Inhibition Of 11 β -Hydroxysteroid Dehydrogenase By Carbenoxolone In Rat Brain Regions And Peripheral Tissues, J. Steroid Biochem. Molec. Biol. (1993) Vol. 46, No. 2, p. 209-213
	BD	H. J. Karl, et al., In Vitro Transformation Of Cortisol By Human Adipose Tissue, Horm. Metab. Res. (1969):1, p. 95
	BE	V. Lakshmi, et al., Regional Distribution Of 11 β -Hydroxysteroid Dehydrogenase In Rat Brain, Endocrinology (1991) Vol. 128, No. 4, p. 1741-1748
	BF	B. Lambert, et al., Effect of Carbenoxolone On Lipolysis In Rat Adipose Tissue, J. Pharm. Pharmac. (1977): 30, p. 301-303
	BG	Joseph Levin, et al., Extraadrenal Effects Of Metirapone In Man, Journal Of Clinical Endocrinology And Metabolism (1978) Vol. 47, No. 4, p. 845-849
	BH	D. E. W. Livingstone, et al., Is 11 β -Hydroxysteroid Dehydrogenase Type 1 A Therapeutic Target? Effects Of Carbenoxolone In Lean And Obese Zucker Rats, Journal Of Pharmacology And Experimental Therapeutics (2003) Vol. 305, No. 1, p. 167-172
	BI	P. Loli, et al., Use of Ketoconazole In The Treatment Of Cushing's Syndrome, Journal Of Clinical Endocrinology And Metabolism (1986) Vol. 63, No. 6, p. 1365-1371
	BJ	Susan C. Low, et al., Glucocorticoids Regulate Hippocampal 11 β -Hydroxysteroid Dehydrogenase Activity And Gene Expression In Vivo In The Rat, Journal Of Neuroendocrinology (1994) Vol. 6, p. 285-290
	BK	Per Marin, et al., Cortisol Secretion In Relation To Body Fat Distribution In Obese Premenopausal Women, Metabolism (1992) Vol. 41, No. 8, p. 882-886
	BL	I. Mineu, et al., Insulinresistance: The Link Between Impaired Glucose Tolerance, Body Mass Index And Plasma Lipids, Rev. Roum. Med. Int. (1993) Vol. 31, No. 4, p. 237-243
	BM	M. Moisan, et al., 11 β -Hydroxysteroid Dehydrogenase Bioactivity And Messenger RNA Expression In Rat Forebrain: Localization In Hypothalamus, Hippocampus, And Cortex, Endocrinology (1990) Vol. 127, No. 3, p. 1450-1455
	BN	C. Monder, et al., 11 β -Hydroxysteroid Dehydrogenase, Vitamins and Hormones (1993) Vol. 47, p. 187-271
	BO	T. Ohno, et al., Metirapone-Induced Thermogenesis In Cold And Heat Acclimated Rats, Japanese Journal Of Physiology (1986): 36, p. 821-825
	BQ	D. Orth, et al., Hyperfunction, The Adrenal Cortex, p. 536-562
	BR	S. J. Quick, et al., Epithelial And Adipose Cells Isolated From mammary Glands Of Pregnant And Lactating Rats Differ In 11 β -Hydroxysteroid Dehydrogenase Activity, J. Steroid Biochem. Molec. Biol. (1990) Vol. 37, No. 4, p. 529-534
	BS	S. J. Quick, et al., 11 β -Hydroxysteroid Dehydrogenase Activity In The Mammary Gland, J. Steroid Biochem. (1990) Vol. 35, No. 6, p. 623-625
	BT	V. Rajan, et al., 11 β -Hydroxysteroid Dehydrogenase In Cultured Hippocampal Cells Reactivates Inert 11-Dehydrocorticosterone, Potentiating Neurotoxicity, Journal Of Neuroscience (1996): 16, (1) p. 65-70
	BU	V. Rajan, et al., Cloning, Sequencing And Tissue-Distribution Of Mouse 11 β -Hydroxysteroid Dehydrogenase-1 cDNA, J. Steroid Biochem. Molec. Biol. (1995) Vol. 52, No. 2, p. 141-147

EXAMINER	DATE CONSIDERED
----------	-----------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Based on Form PTO-1449 (3/90) LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)	ATTY. DOCKET NO. 674543-2001.5	SERIAL NO. 10/080,787
	APPLICANT Brian Robert Walker	
	FILING DATE February 22, 2002	GROUP 1617

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

	BV	P. W. Raven, et al., Extra-Adrenal Effects Of Metyrapone Include Inhibition Of The 11-Oxoreductase Activity Of 11 β -Hydroxysteroid Dehydrogenase: A Model For 11-HSD 1 Deficiency, Clinical Endocrinology (1995) Vol. 43, p. 634-644
	BW	R. Sanpath-Kumar, et al., Metyrapone Is A Competitive Inhibitor Of 11 β -Hydroxysteroid Dehydrogenase Type 1 Reductase, J. Steroid Biochem. Molec. Biol (1997) Vol. 62, No. 23, p. 195-199
	BX	Program Abstracts Philadelphia, Endo 2003, June 19-22, 2003, p. 101
	BY	T. C. Sandeep, et al., Increased In Vivo Regeneration Of Cortisol In Adipose Tissue In Human Obesity And Effects Of The 11 β -Hydroxysteroid Dehydrogenase Type 1 Inhibitor Carbenoxolone, Diabetes (2005) Vol. 54, p. 872-879
	BZ	R. M. Sapolsky, et al., Prolonged Glucocorticoid Exposure Reduces Hippocampal Neuron Number: Implications For Aging, Journal Of Neuroscience (1985) Vol. 5, No. 5, p. 1222-1227
	CA	R. M. Sapolsky, A Mechanism For glucocorticoid Toxicity In The hippocampus: Increased Neuronal Vulnerability To Metabolic Insults, Journal Of Neuroscience (1985) Vol. 5, No. 5, p. 1228-1232
	CB	R. M. Sapolsky, Glucocorticoid Toxicity In The Hippocampus, Neuroendocrinology (1986) Vol. 43, p. 440-444
	CC	D. S. Schade, et al., Modulation Of Basal Ketone Body Concentration By Cortisol In Diabetic Man, Journal Of Clinical Endocrinology And Metabolism (1978) Vol. 47, No. 3, p. 519-528
	CD	J. R. Seckl, Glycyrhethinic Acid, An Inhibitor Of 11 β -Hydroxysteroid Dehydrogenase, Alters Local Cerebral Glucose Utilization In Vivo, J. Steroid Biochem. Molec. Biol. (1991) Vol. 39, No. 5A, p. 777-779
	CE	J. R. Seckl, 11 β -Hydroxysteroid Dehydrogenase Isoforms And Their Implications For Blood Pressure Regulation, European Journal Of Clinical Investigation (1993) Vol. 23, p. 589-601
	CF	N. Sonino, et al., Ketoconazole Treatment In Cushing's Syndrome: Experience In 34 Patients, Clinical Endocrinology (1991) Vol. 35, p. 347-352
	CG	P.M. Stewart, et al., Mineralocorticoid Activity Of Carbenoxolone: Contrasting Effects Of Carbenoxolone And Liqueurice On 11 β -Hydroxysteroid Dehydrogenase Activity In Man, Clinical Science (1990) Vol. 78, p. 49-54
	CH	P. M. Stewart, et al., The Cortisol-Cortisone Shuttle And Hypertension, J. Steroid Biochem. Molec. Biol. (1991) Vol. 40, No. 4-6, p. 501-509
	CI	B. A. Stein, et al., Chemical Adrenalectomy Reduces Hippocampal Damage Induced By Kainic Acid, Brain Research (1988) Vol. 473, p. 175-180
	CJ	A. Tabarin, et al., Use Of Ketoconazole In The Treatment Of Cushing's Disease And Ectopic ACTH Syndrome, Clinical Endocrinology (1991) Vol. 34, p. 63-69
	CK	J. Thakore, et al., Cortisol Synthesis Inhibition: A New Treatment Strategy For The Clinical And Endocrine Manifestations Of Depression, Society Of Biological Psychiatry (1995) Vol. 37, p. 364-368
	CL	M. Thorén, et al., Aminoglutethimide And Metyrapone In The Management Of Cushing's Syndrome, Acta Endocrinologica (1985) Vol. 109, p. 451-457
	CM	J. A. Verheist, et al., Short And Long-Term Responses To Metyrapone In the Medical Management Of 91 Patients With Cushing's Syndrome, Clinical Endocrinology (1991) Vol. 35, p. 169-178
	CN	S. M. Virtanen, et al., Dietary Factors In The Aetiology Of Diabetes, Ann. Med. (1994) Vol. 26, p. 469-478
	CO	B. R. Walker, et al., Deficient Inactivation Of Cortisol By 11 β -Hydroxysteroid Dehydrogenase In Essential Hypertension, Clinical Endocrinology (1993) Vol. 39, p. 221-227
	CP	B. R. Walker, et al., Carbenoxolone Increases Hepatic Insulin Sensitivity In Man: A Novel Role For 11-Oxosteroid Reductase In Enhancing Glucocorticoid Receptor Activation, Journal Of Clinical Endocrinology And Metabolism (1995) Vol. 80, No. 11, p. 3155-3159
	CQ	J. Weidenfeld, et al., In Vitro Metabolism Of Cortisol By Human Abdominal Adipose Tissue, J. Steroid Biochem. (1982) Vol. 17, p. 357-360

EXAMINER	DATE CONSIDERED
----------	-----------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

GROUP 1617

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
---------------------	-----------------	------	------	-------	----------	-------------------------------

FILING DATE
IF APPROPRIATE

YES	NO
-----	----

C. De Martinis, Modificazioni Della Tolleranza Al Glucosio Dopo Metopirone In Soggetti Normali E Diabetici Osservazioni Preliminari, Della Societa Italiana Di Biologia Sperimentale (1963) Vol. XXXIX, No. 6, p. 372-374

DATE CONSIDERED

* **EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.